

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 6,899,915 B2
APPLICATION NO. : 09/997734
DATED : May 31, 2005
INVENTOR(S) : Dunn

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It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Delete Title page illustrating figure, and substitute new Title page illustrating figure attached.

Delete drawing sheets 1-20, and substitute drawing sheets 1-20, with the attached sheets.

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Eighth Day of August, 2006

A handwritten signature in black ink, reading "Jon W. Dudas". The signature is stylized, with a large loop for the "J" and a cursive "Dudas".

JON W. DUDAS
Director of the United States Patent and Trademark Office

(12) **United States Patent**
Yelick et al.

(10) Patent No.: **US 6,899,915 B2**
(45) Date of Patent: **May 31, 2005**

(54) **METHODS AND COMPOSITIONS FOR CULTURING A BIOLOGICAL TOOTH**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: 09/997,734

(22) Filed: Nov. 29, 2001

(65) Prior Publication Data

US 2002/0119180 A1 Aug. 29, 2002

Related U.S. Application Data

(60) Provisional application No. 60/253,891, filed on Nov. 29, 2000.

(51) Int. Cl.⁷ A61C 13/08

(52) U.S. Cl. 427/2.26; 433/202.1; 433/204; 264/19; 523/115

(58) Field of Search 427/2.26, 2.27; 433/202.1, 204, 215, 223; 264/19; 523/115; 521/50, 51, 55; 514/21; 424/435; 623/23.58, 23.72, 23.75

(56) **References Cited**

U.S. PATENT DOCUMENTS

5,098,891 A * 3/1992 Hammarstrom et al. 514/21
5,418,221 A * 5/1995 Hammarstrom et al. 514/21
5,863,297 A * 1/1999 Walter et al. 623/17.18

5,885,829 A * 3/1999 Mooney et al. 435/325
6,488,503 B1 * 12/2002 Lichkus et al. 433/202.1
2002/0022883 A1 * 2/2002 Burg 623/8
2002/0192198 A1 * 12/2002 Elia 424/93.21

OTHER PUBLICATIONS

"Annual Industry Report," *Implant Dentistry*, 9(3):192-194 (2000).

Baba et al., "Determination of enamel protein synthesized by recombined mouse molar tooth germs in organ culture," *Archives of Oral Biology* 41:215-219 (1996).

Backman et al., "Amelogenesis imperfecta: prevalence and incidence in a northern Swedish country," *Community Dent Oral Epidemiol*, 14(1):43-47 (1986).

Choi et al., "Studies of brush border enzymes, basement membrane components, and electrophysiology of tissue-engineered neointestine," *J. Pediatr. Surg.* 33:991-6; discussion 996-997 (1998).

(Continued)

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Assistant Examiner—Melanie Bissett

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(57)

ABSTRACT

Tooth tissues include the pulp mesenchyme that forms the dentin and an epithelium that is responsible for enamel formation. Cells from these tissues were obtained from porcine third molars and were seeded onto a biodegradable scaffold composed of a polyglycolic acid—polylactic acid copolymer. Cell polymer constructs were then surgically implanted into the omentum of athymic nude rats so that the constructs would have a blood supply and these tissues were allowed to develop inside the rats. Infrequently, columnar epithelial cells were observed as a single layer on the outside of the dentin-like matrix similar to the actual arrangement of ameloblasts over dentin during early tooth development. Developing tooth tissues derived from such cell polymer constructs could eventually be surgically implanted into the gum of an edentulous recipient where the construct would receive a blood supply and develop to maturity, providing the recipient with a biological tooth replacement.

54 Claims, 20 Drawing Sheets

Tooth Scaffolds



PGA + PLLA



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Tooth Scaffolds

PGA + PLLA



Fig. 1

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Tooth Scaffolds-PLGA

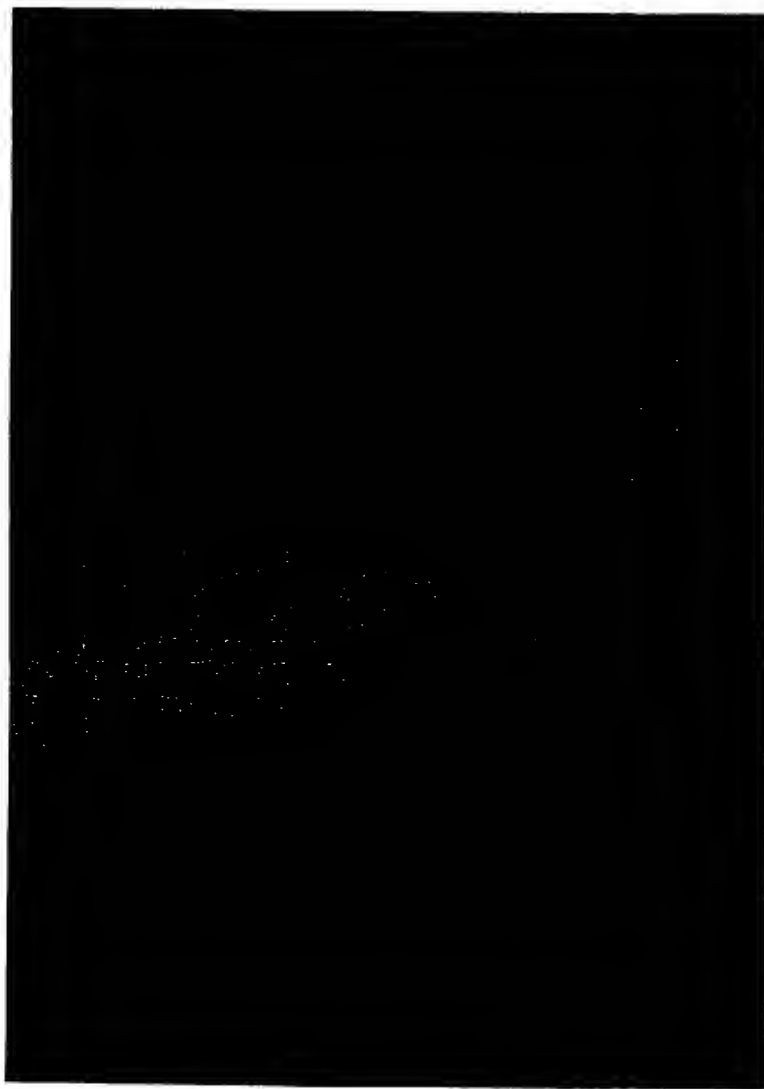


Fig. 2

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SEM-PLGA Scaffold + Salt

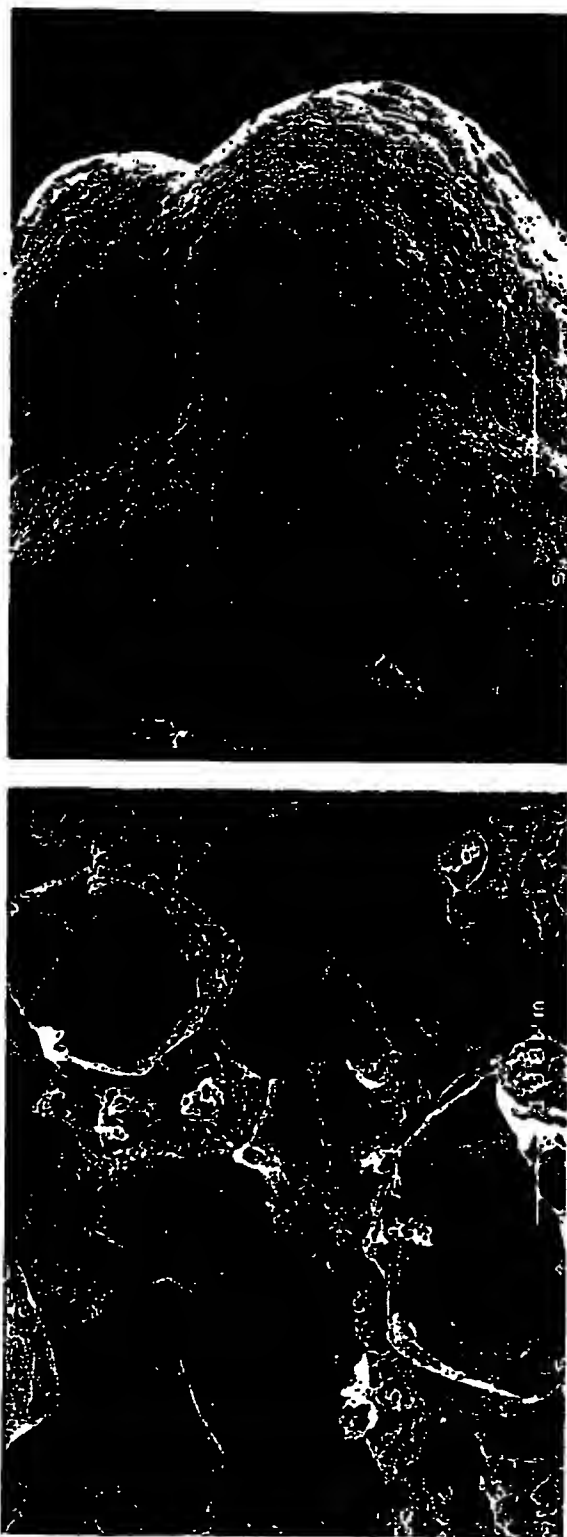


Fig. 3

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SEM-PLGA Scaffold + Sugar

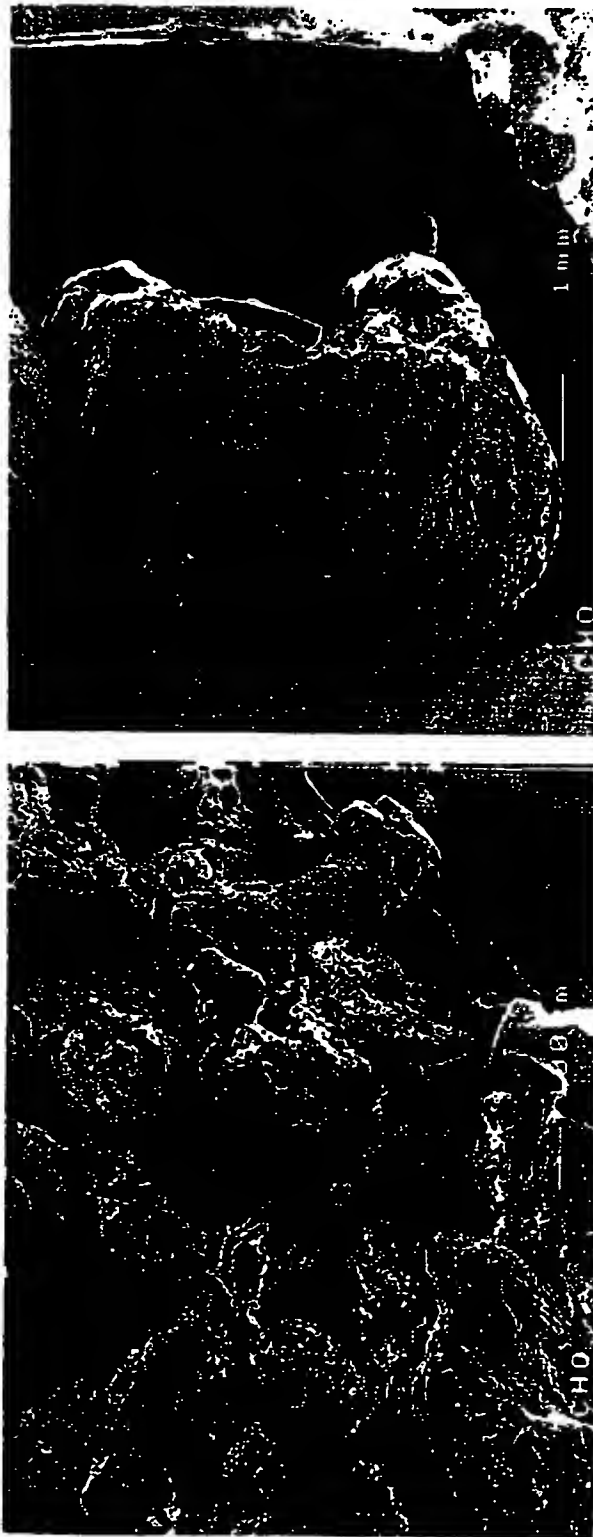


Fig. 4

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Removal of Porcine Third Molar



Fig. 5

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Removal of Porcine Third Molar



Fig. 6

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Porcine Tooth Tissue Culture

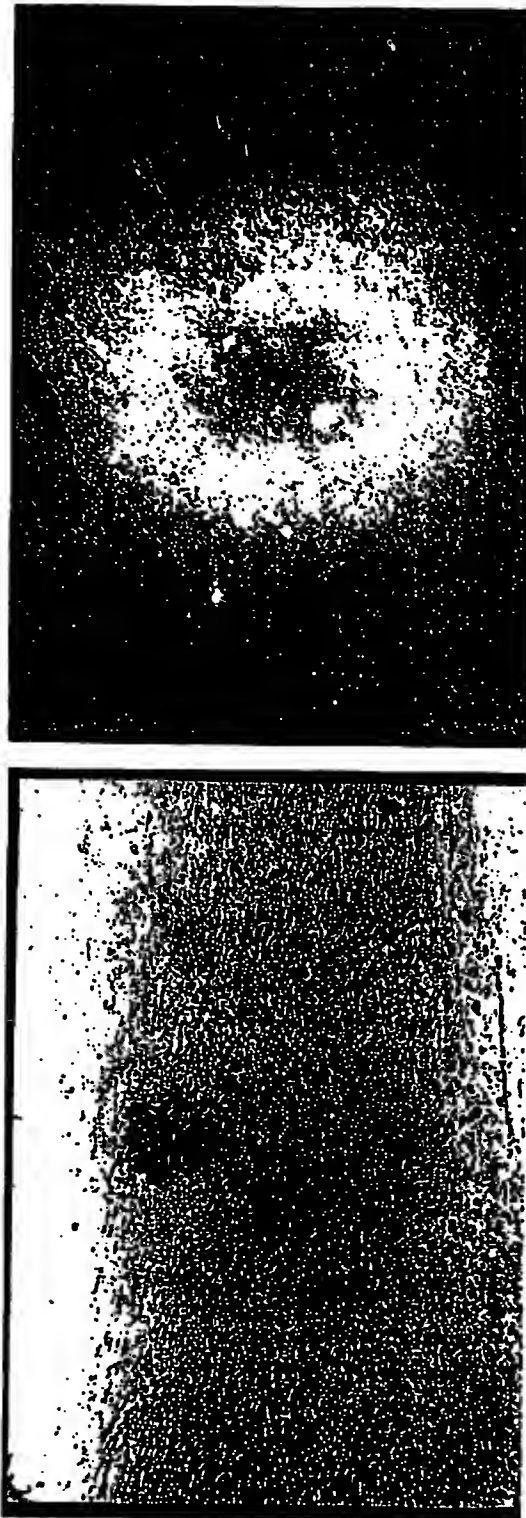


Fig. 7

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Tissue Culture-Von Kossa Stain

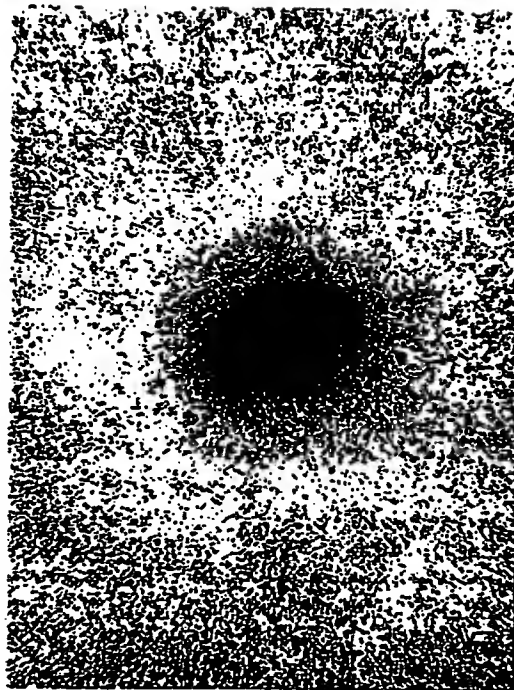
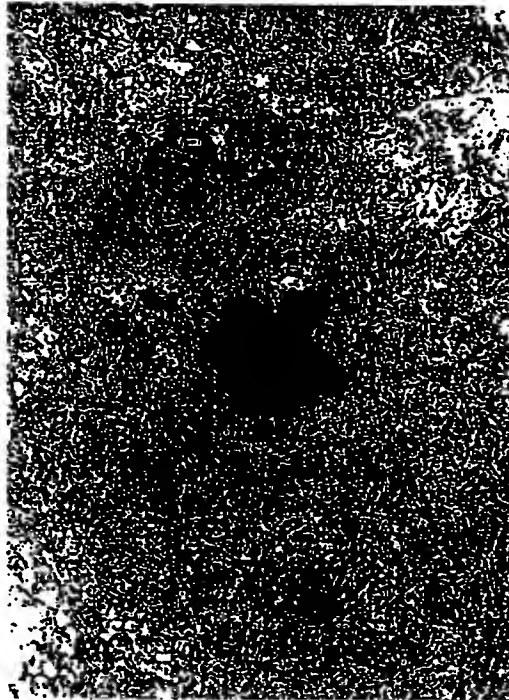


Fig. 8

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Rat Radiographs - Human Tooth

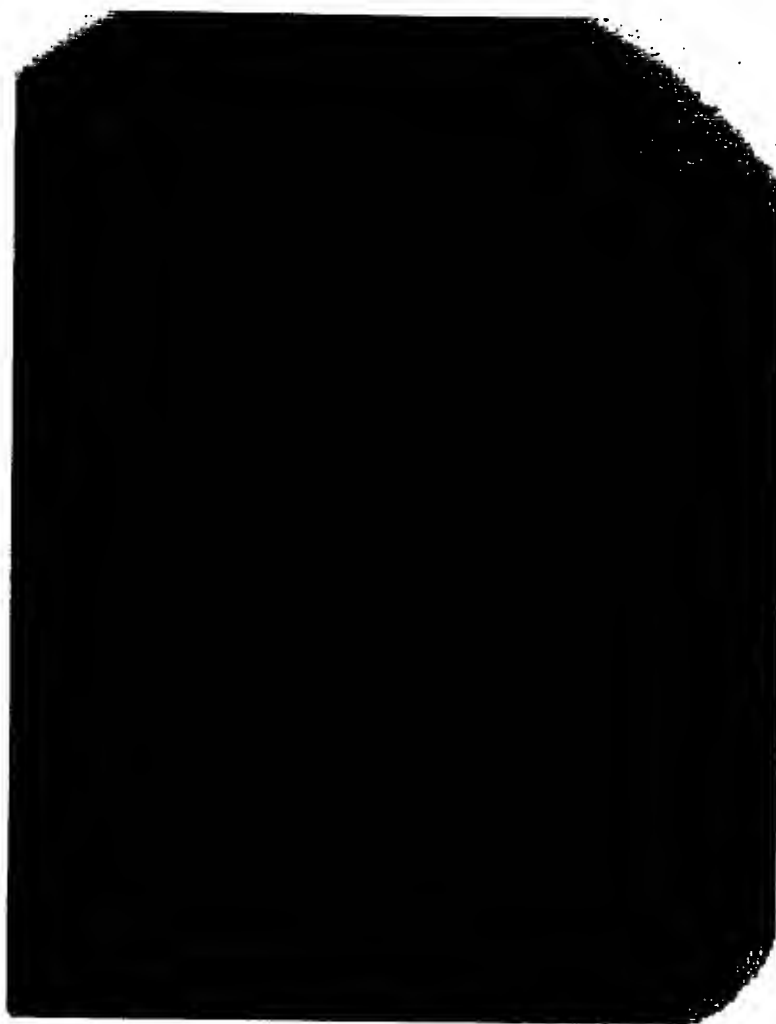


Fig. 9

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Rat Radiographs - Implant, 7.5 weeks

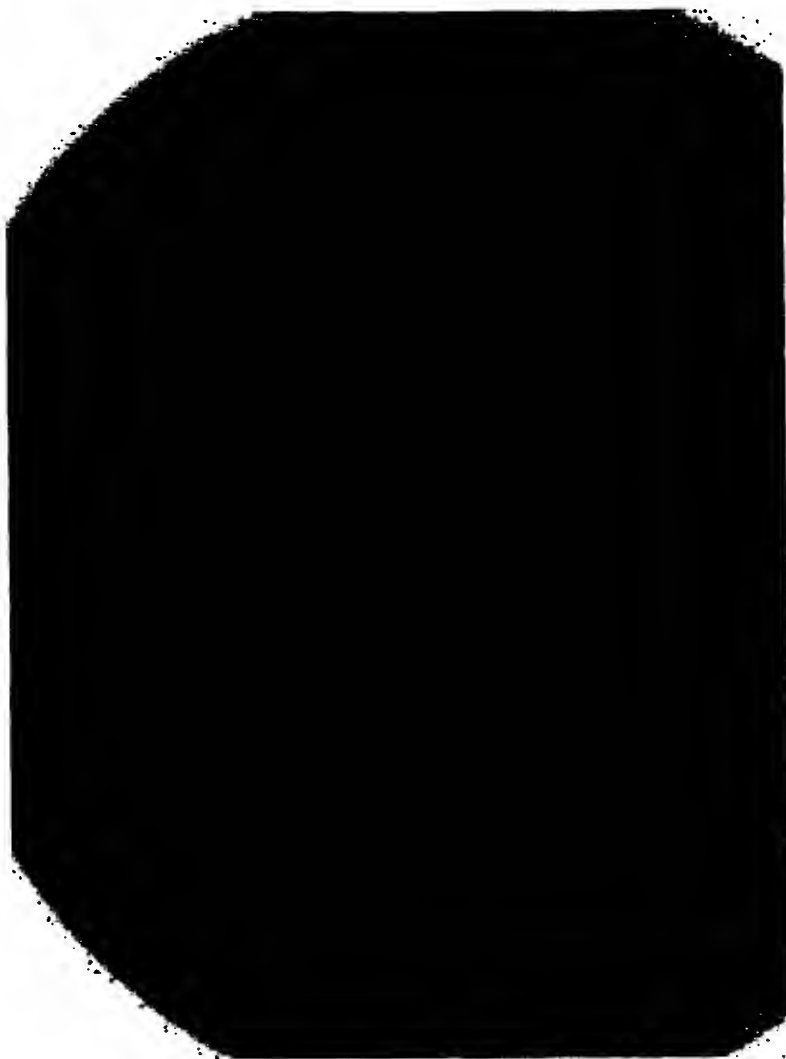


Fig. 10

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Dissection of Tissue



Fig. 11

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Dissection of Tooth Tissue
7.5 weeks



Fig. 12

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Dissected Tooth Tissue - 7.5 Weeks



Fig. 13

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Dissected Tooth Tissue Cysts - 7.5 Weeks



Fig. 14

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Tissue Samples Were Sectioned

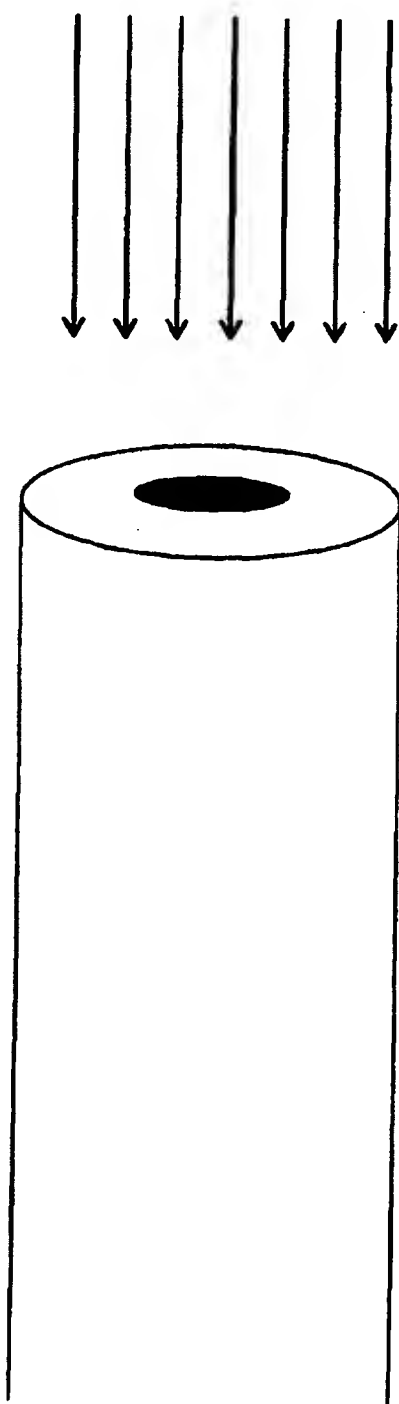


Fig. 15

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Goldner's Stain
Green = mineralized tissue



Fig. 16

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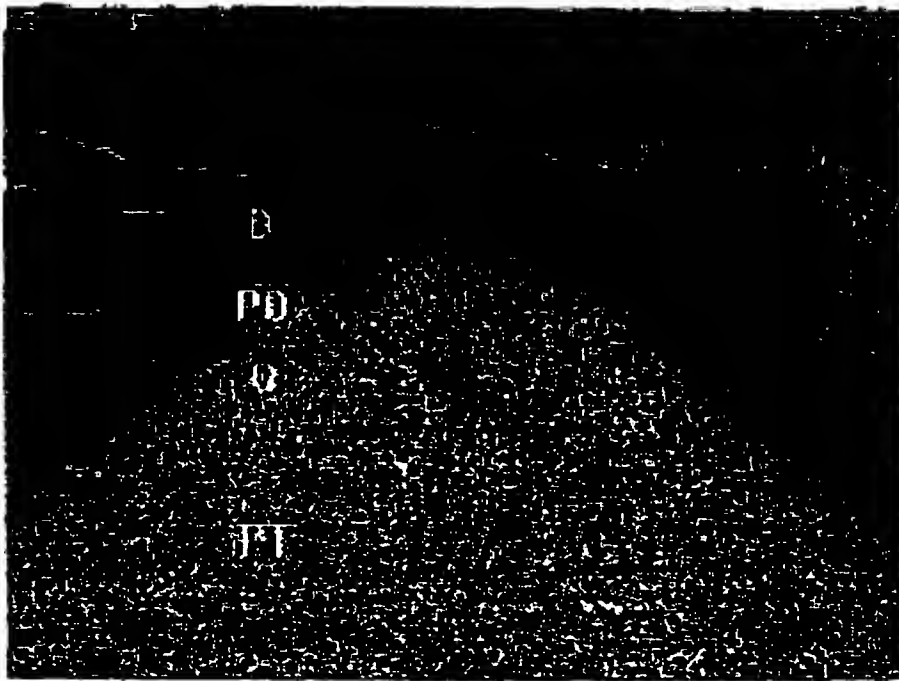


Fig. 17

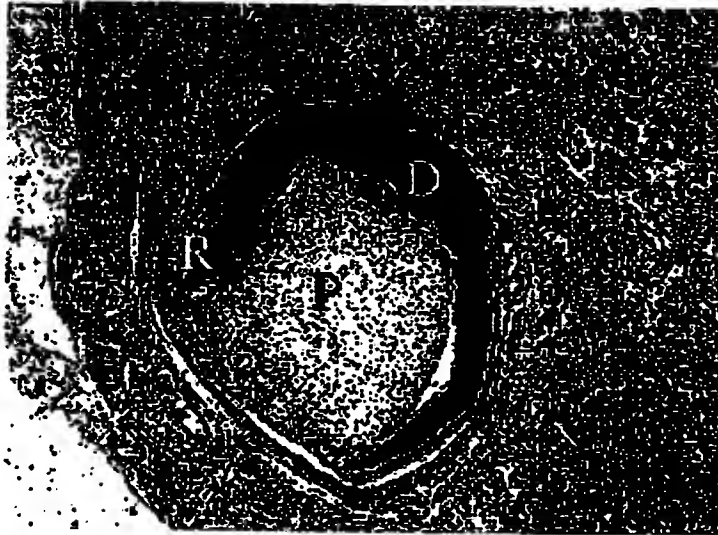
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A



B

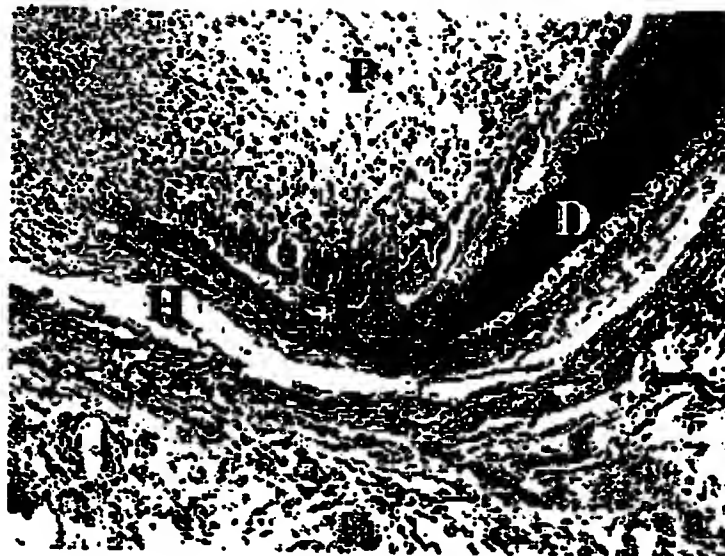


Fig. 18

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A



B



Fig. 19

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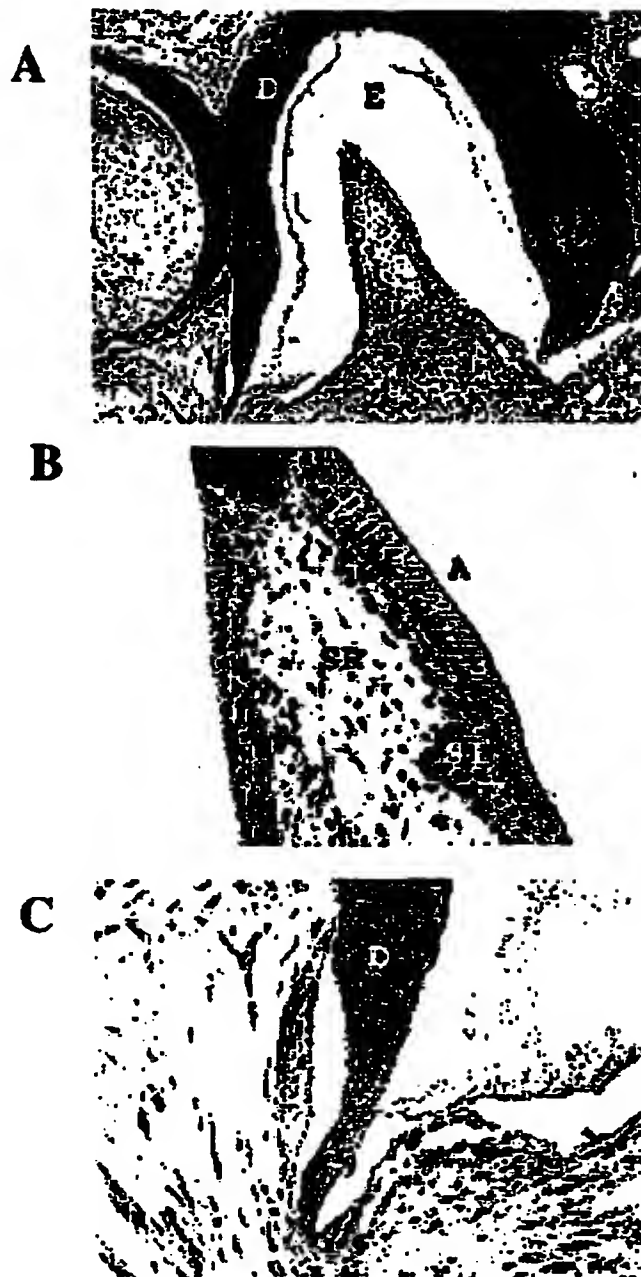


Fig. 20

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